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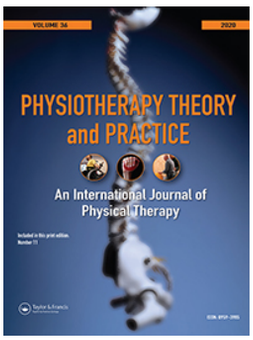

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The effects of various respiratory physiotherapies after lung resection: a systematic review

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ABSTRACT

Purpose: The purpose of this review was to investigate the effect of respiratory physiotherapy after lung resection on mortality, postoperative pulmonary complications (PPC), length of stay, lung volumes, and adverse events.

Material and methods: Randomized or quasi-randomized controlled trials were searched in CENTRAL, PubMed, EMBASE, Cinahl, PEDro, and hand searching of related studies. Various respiratory physiotherapy interventions were compared to standard care, sham treatment, or no treatment. Two reviewers assessed eligibility and quality of studies using Cochrane guidelines. Meta-analyses were undertaken on subgroups of intervention.

Results: Various types of positive pressure breathing, deep breathing exercises, and strength and aerobic exercises as a supplement to standard care did not show any significant effect over standard care in preventing mortality or PPC, reducing length of stay, or improving lung volumes.

Conclusion: Prophylactic continuous positive airway pressure does not seem to affect rate of mortality and PPC, when compared with standard care embodying respiratory physiotherapy such as airway clearance techniques and assistance with early ambulation. However, further research is still needed to make a final conclusion. The effect of standard respiratory physiotherapy as a package is still unknown, and may or may not be effective in preventing PPC among patients undergoing lung resection.

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KEYWORDS
Systematic review; lung resection; thoracotomy; postoperative pulmonary complications; physiotherapy

Introduction

Within the Western world lung cancer remains the leading cause of cancer death. The primary curative treatment is lung resection surgery (Siegel, Miller, and Jemal, 2015). The surgery involves a high risk of sustaining postoperative pulmonary complications (PPC), which are associated with increased length of stay (LOS), intensive care unit admission, and mortality (Sachdev and Napolitano, 2012). The reported incidence of PPC varies from 15% (Dales et al., 1993) to 37% (Sachdev and Napolitano, 2012). Generally, PPC include conditions, such as significant hypoxia and atelectasis, pneumonia, exacerbation of Chronic Obstructive Pulmonary Disease (COPD), various types of upper airway obstruction, pulmonary edema, and tracheal re-intubation (Ireland et al., 2014; Sachdev and Napolitano, 2012). Known factors associated with increased risk of PPC are extended pulmonary resections, preoperative chemotherapy, and comorbidity (Bernard et al., 2000).

Respiratory physiotherapy comprises many different treatment techniques that generally aims at optimizing ventilation and clearing airway secretions in order to improve gas exchange and make breathing easier (Frownfelter and Dean, 2012; Reeve, Denehy, and Stiller, 2007). Typically used components of respiratory physiotherapy are ambulation, position change, and breathing techniques. All of these are used to improve respiratory function postoperatively by increasing ventilation and functional residual capacity, thus avoiding lung volumes below closing capacity (Fagevik Olsen, Lannefors, and Westerdahl, 2015). Breathing techniques involving positive expiratory pressure (PEP) change the breathing pattern, and has been shown to increase functional residual capacity (Fagevik Olsen, Lannefors, and Westerdahl, 2015). The increased positive pressure during breathing is believed to reinflate collapsed alveoli, allowing pressure to build up distal to the obstruction, and by promoting the movement of pulmonary

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secretions towards larger airways (Mejja-Downs, 2012). Some airway clearance techniques include different types of vibration, which is believed to decrease collapsibility of the airways and to promote loosening pulmonary secretions (Mejja-Downs, 2012). Other treatments such as exercises for the upper extremities and thorax mobility techniques are believed to enable a more freely chest wall excursion necessary for a normal breathing pattern and thereby improving oxygenation (Frownfelter, 2012).

To our knowledge, two reviews (Rodriguez-Larrad, Lascurain-Aguirrebena, Abecia-Inchaurregui, and Seco, 2014; Varela, Novoa, Agostini, and Ballesteros, 2011) have investigated the effect of respiratory physiotherapy on PPC and mortality after lung resection. Both reviews commented on the lack of well-designed clinical trials and made no firm conclusion (Rodriguez-Larrad, Lascurain-Aguirrebena, Abecia-Inchaurregui, and Seco, 2014; Varela, Novoa, Agostini, and Ballesteros, 2011). However, one review did not use systematic methods (Varela, Novoa, Agostini, and Ballesteros, 2011) and the other did only use search terms focusing on exercise (Rodriguez-Larrad, Lascurain-Aguirrebena, Abecia-Inchaurregui, and Seco, 2014), for which reason relevant studies may have been missed. Overall, substantial resources are spent on respiratory physiotherapy after lung resection in order to prevent PPC and thereby reduce mortality and LOS. Therefore, it is relevant to investigate whether respiratory physiotherapy after lung resection is effective and how strong the evidence is (Reeve, Denehy, and Stiller, 2007). Therefore, it is relevant to conduct a systematic review of all literature on the topic in order to include studies missing in previous reviews or newly published studies (Reeve, Denehy, and Stiller, 2007). Furthermore, it is conceivable that patients in high risk of PPC may profit more from respiratory physiotherapy than patients in low risk of PPC, which would call for further knowledge on treatment effect among risk groups to create a more differentiated treatment strategy. Consequently, the overall objective of this study was to investigate the effect of respiratory physiotherapy after lung resection surgery on rate of mortality and PPC, and to investigate different types of respiratory physiotherapy and the effect among different risk subgroups of PPC.

Methods

Preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines and the Cochrane Handbook for Systematic Reviews of Intervention were followed in this review (Higgins and Green, 2011; Moher et al., 2015). As recommended in the guidelines, to assist transparency of the used methods and processes of the review, a protocol was published ahead of this review (Andersen et al., 2017). Furthermore, the review was registered with the International Prospective Register of Systematic Reviews (PROSPERO) on October 10, 2016 (registration number CRD42016048956).

Criteria for considering studies for this review

Study designs included in the review were randomized and quasi-randomized controlled trials. Participants included in the review were all adults who received respiratory physiotherapy after scheduled lung resection surgery by open thoracotomy or video-assisted thoracoscopic surgery (VATS). Studies addressing thoracic surgeries other than lung resection were excluded unless data for patients undergoing lung resection was reported separately.

Interventions included in the review were any type of postoperative respiratory physiotherapy applied during hospital stay (e.g. huffing, coughing, breathing exercises with or without applied positive pressure, postural drainage, percussion, vibration and shaking, and mobilization or physical exercise targeted at improving pulmonary function and preventing PPC). Studies investigating preoperative or outpatient interventions were excluded, unless outcomes evaluating the postoperative intervention during hospital stay were reported separately. Comparisons of interventions were standard care defined by the individual studies, sham treatment, or no treatment.

Primary outcomes of the review were mortality within 30 days and PPCs as defined in the individual studies. Secondary outcomes were LOS, lung volume and function, and adverse events (i.e any undesired outcome due to the intervention).

Search methods and study selection

The search for literature included Cochrane Central of Trials (CENTRAL), PubMed, EMBASE, Cinahl, and the Physiotherapy Evidence Database (PEDro). The search strategies were inspired by a search strategy for randomized controlled trials constructed and validated by Cochrane (Lefebvre, Manheimer, and Glanville, 2008). No language or date limits were used. The search strategy of PubMed (Table 1) was adapted to search the above-mentioned databases (see supplemental online material), and all searches were reviewed by a health information specialist. Trial registers (ClinicalTrials.gov and ISRCTN) were searched for ongoing and completed trials. We consulted reference lists of relevant

Table 1. Search strategy of PubMed.

	AND		
OR	Population	Intervention	Study design*
	Pulmonary surgical procedure [mh] [tiab] (p) Thoracotomy [mh] [tiab] (p) Thoracic surgery [mh] [tiab] (p) Video-assisted thoracic surgery [mh] [tiab] (p) Video-assisted thorascopic surgery [tiab] (p) Lung surgery [tiab] (p) Lung resectional surgery [tiab] (p) Lung resection [tiab] (p) Lung volume reduction surgery [tiab] (p) Lobectomy [tiab] (p)	Respiratory physiotherapy [tiab] Respiratory physical therapy [tiab] Chest physiotherapy [tiab] Chest physical therapy [tiab] Lung physiotherapy [tiab] Lung physical therapy [tiab] Continuous positive airway pressure [mh] [tiab] CPAP [tiab] Noninvasive ventilation [mh] [tiab] Bilevel positive airway pressure [tiab] Biphasic positive airway pressure [tiab] Positive expiratory pressure [tiab] Intermittent positive pressure breathing [mh] [tiab] Inspiratory muscle training [tiab] Airway clearance technique [tiab] (p) Breathing exercises [mh] [tiab] (p) Incentive spirometry [tiab] Sustained maximal inspiration [tiab] Postural drainage [tiab] Autogenic drainage [tiab] Bronchial drainage [tiab] Bronchial hygiene [tiab] ELTGOL [tiab] Forced expiratory technique [tiab] (p) Early ambulation [mh] [tiab] Early mobilization [tiab]	Randomized controlled trial [pt] Controlled clinical trial [pt] Randomized [tiab] Randomized [tiab] Placebo [tiab] Randomly [tiab] Trial [tiab] Groups [tiab] Control group [tiab] NOT Animals [mh] not (humans[mh] and animals [mh])

AND, OR, NOT denotes boolean operators.
[mh] denotes MeSH term (exploded).
[tiab] denotes search in title and abstract.
[pt] denotes search in publication type.
(p) denotes search in both single and plural.
*Inspired by *Cochrane Highly Sensitive Search Strategy for identifying randomized trials in MEDLINE (reference).*

articles to identify additional studies that were not identified during the systematic literature search.

Two review authors (KSL and BS) performed the first selection of studies based on titles and abstracts. Studies considered potentially relevant were read independently in full text in order to determine the eligibility for the present review. Disagreements between reviewers were resolved by discussion and consensus, and if necessary a third author (AKP) resolved remaining differences. The reference management software Refworks was chosen for managing the records retrieved from the searches in databases.

Data collection and analysis

Two review authors extracted data independently (KSL and BS), using a standard data collection form, which was tested by three authors (KSL, BS, and AKP) before initiating the process of data extraction and quality assessment of the included studies. Any disagreements were resolved by discussion and consensus, and if necessary resolved by a third author (AKP). Multiple reports of the same study were collated and considered as one study. These criteria were scored as 'positive', 'negative', or 'unclear'. We contacted trial authors for additional information if items were scored 'unclear'. Guidelines of the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group were used to rate the overall quality of evidence of meta-analyses (Schünemann et al., 2008).

The Cochrane tool for risk of bias was used to assess the following domains: Random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias (Higgins and Altman, 2008). Blinding of participants and personnel is impossible in trials of physiotherapy. Therefore, studies were classified as low risk of bias if the domains besides blinding of participants and personnel were considered adequate; as high risk of bias if one or more of these domains were inadequate and if plausible biases seriously weakened confidence in the results. If one or more of these domains were considered unclear and plausible biases raised some doubt about the results, the study was evaluated as unclear risk of bias.

In case of dichotomous outcomes, the treatment effect was measured as risk ratios (RR) with 95% confidence intervals (CIs). Continuous outcomes were measured as mean differences (MDs) with 95% CIs or

as standardized mean differences (SMDs) if different methods of measurement were used in the studies.

We contacted trial authors in order to request additional information and obtain missing data. Assumptions were made on whether missing data in the included studies were random and whether the authors had dealt with missing data appropriately. Sensitivity analysis was performed to assess how sensitive results were changing (Higgins, Deeks, and Altman, 2008).

Clinical heterogeneity was evaluated by the degree of differences of intervention or patient characteristics. Methodological heterogeneity was evaluated by the variation in risk of bias. The quantity of statistical heterogeneity was evaluated by I2 statistics (Deeks, Higgins, and Altman, 2008).

Potential reporting biases were assessed by funnel plot if the number of studies was sufficient (≥10 studies) (Sterne et al., 2011). Furthermore, ClinicalTrials.gov and ISRCTN registries were screened for completed but unpublished studies. If available, the trial protocol was compared to the published report in order to evaluate outcome reporting bias in the individual study.

Data synthesis and analysis

Meta-analyses were performed in the software RevMan 5.3 if considered possible. The fixed-effect model was used if data was considered homogeneous. Clinical homogeneity was a prerequisite for pooling studies. A random-effects model was used to summarize the results if the I2 statistic were >50%. If meta-analyses were not undertaken, a narrative synthesis of the available data was provided in text and tables to summarize characteristics and findings of the studies.

When possible, the following subgroup analyses were performed on type of intervention: continuous positive airway pressure (CPAP) including bi-level pressure (BIPAP) more than 30 minutes; breathing exercises including breathing with or without intermittent positive pressure; physical exercise including ambulation; and targeted respiratory physiotherapy including multiple techniques. To evaluate whether the effect of respiratory physiotherapy differs between groups, additional subgroup analyses were performed on population with low versus high risk of PPC (as defined by the individual studies).

If sufficient data was available, sensitivity analyses were carried out in the following: study quality (high risk of bias versus low risk of bias); missing data (observed and imputed data versus observed data only); study size (stratified by sample size of under and over 100 participants); allocation concealment (high risk of bias versus low risk of bias); and assessor blinding (high risk of bias versus low risk of bias).

Results

The main literature search was performed on March 24, 2017, and resulted in a total of 1192 references (Figure 1), of which 11 were included in the review. The literature search in databases provided 11 studies (Agostini et al., 2013; Aguiló et al., 1997; Arbane et al., 2014; Barbagallo et al., 2012; Frolund and Madsen, 1986; Garutti et al., 2014; Lorut et al., 2014; Ludwig et al., 2011; Nery et al., 2012; Reeve et al., 2010; Roceto, Galhardo, Saad, and Toro, 2014). Additionally, two studies (Arbane, Tropman, Jackson, and Garrod, 2011; Danner et al., 2012) were identified from the reference list of a relevant article.

One study investigating CPAP compared to standard care was identified in the ISRCTN registry (No. 13454737) but the study has not yet been published. Finally, 13 trials were included in the review (Table 2).

Characteristics of studies

Study design

Eleven studies were randomized controlled trials and two studies (Ludwig et al., 2011; Nery et al., 2012) quasi-randomized (Table 2).

Population

The included studies recruited a total of 1280 patients scheduled for lung surgery with a mean age between 51.9 (SD 5.5) (Aguiló et al., 1997) and 71.1 (SD 7.7) (Danner et al., 2012); approximately, 65% in the intervention group and 66% in the control group were male. Two studies included patients undergoing VATS (Arbane et al., 2014; Arbane, Tropman, Jackson, and Garrod, 2011). Three studies included patients undergoing explorative thoracotomy (Agostini et al., 2013; Aguiló et al., 1997; Frolund and Madsen, 1986). Six studies also included patients undergoing lung surgery for reasons other than lung cancer (Agostini et al., 2013; Aguiló et al., 1997; Frolund and Madsen, 1986; Lorut et al., 2014; Nery et al., 2012; Reeve et al., 2010). Two studies solely investigated patients at higher risk of PPC defined by either guidelines of the British Thoracic Society or diagnosis of moderate to severe COPD (Danner et al., 2012; Lorut et al., 2014).

Setting

All studies recruited patients at the hospitals where the surgery was performed. Two studies (Arbane et al., 2014; Lorut et al., 2014) were multicenter-trials and had stratified the randomization per center; no cluster

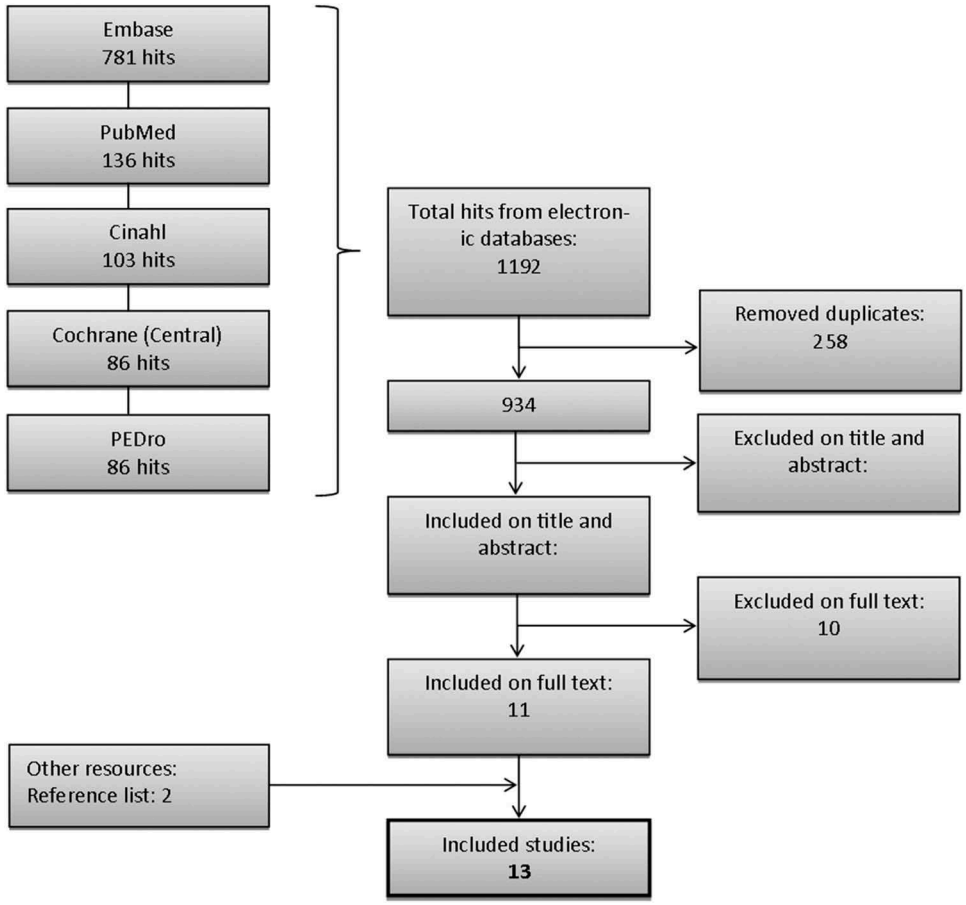

Figure 1. Flow chart of literature search results.

analyses were performed. Two studies (Arbane et al., 2014; Arbane, Tropman, Jackson, and Garrod, 2011) combined the hospital intervention with a succeeding home exercise program, but only the outcomes evaluating the intervention during hospital stay were included in the analyses of this review.

Intervention

Seven trials investigated CPAP, of which two trials used BIPAP (Aguiló et al., 1997; Lorut et al., 2014). The total duration of CPAP treatments ranged from 1 hour (Aguiló et al., 1997) to a mean of 25.6 hours (SD 14.8) (Danner et al., 2012) (Table 3). Three trials investigated breathing exercises with a device (incentive spirometry (Agostini et al., 2013), PEP (Frolund and Madsen, 1986), and intermittent positive pressure breathing (Ludwig et al., 2011)). The intervention period started on the first postoperative day and continued until the third day (Frolund and Madsen, 1986) or until hospital discharge (Agostini et al., 2013; Ludwig et al., 2011). Two trials of the same author investigated physical exercise including walking, minimum 5 minutes of bike exercises, and leg strength training from the first to the fifth postoperative day or until discharge (Arbane et al., 2014; Arbane, Tropman, Jackson, and Garrod, 2011). One study investigated targeted respiratory physiotherapy including deep breathing and coughing exercises, assistance with ambulation (Reeve et al., 2010). The total duration of intervention was a median of 6 hours (30 minutes to 23 hours).

All trials investigated types of respiratory physiotherapy as an additional intervention to standard care. In three studies, standard care comprised standardized surgical and medical management (Aguiló et al., 1997; Garutti et al., 2014; Reeve et al., 2010), of which two studies did not describe whether standard care entailed respiratory physiotherapy (Aguiló et al., 1997; Garutti et al., 2014). In the remaining 10 studies, respiratory physiotherapy in form of assistance with ambulation, coughing, and breathing exercises were described as a component of standard care (Table 2). One trial compared the intervention with standard care and a sham treatment (Frolund and Madsen, 1986).

Studies excluded on basis of title and abstract (Brocki et al., 2016; Chang et al., 2014; Chatham, Marshall, Campbell, and Prescott, 1993; Cho et al., 2014;

Table 2. Characteristics of included studies [ordered by author and year of publication].

Author (year) Country, study design	Participants numbers, sample loss and compliance, age and sex	Intervention type and doses	Comparison Standard care, sham or no treatment	Outcomes measurements and time points	Results
Agostini et al. (2013) United Kingdom *RCT*	180 patients undergoing lung resection via thoracotomy *Sample loss*: 18 (IG) and 14 (CG) missing on lung function, 4 (IG) and 1 (CG) missing on PPC *Compliance*: Unknown if the use of IS were followed when unsupervised *Age (years)*: IG: 65 (IQR: 14) CG: 70 (IQR: 9) *Sex*: IG: 45 M/47 F CG: 41 M/47 F	IS (device offering visual feedback when performing thoracic exercises) minimum of 10 breaths for every waking h (supervised by physiotherapist twice daily) And standard care	*Standard care*: Treatment included thoracic expansion exercises (deep breathing), coughing, early mobilization and active shoulder exercises	*Time points*: Once during follow-up: • LOS • Mortality (within discharge) Daily: • PPC (≥4 of: Atelectasis, elevated white blood cell count or use of respiratory antibiotics, temperature >38 C, sign of infection on sputum microbiology, oxygen saturation <90% on room air, purulent sputum production, diagnosis of pneumonia, readmission to ICU due to respiratory problems) POD 4: • Lung function (FEV1% of preoperative value)	*IG versus CG*: Mortality: 0 (0%) versus 1 (1.1%) PPC (%): *POD 2 and thereafter*: Mean difference between groups of 2.5% (CI95%: −7.9; 12.9), $p = 0.803$ LOS: 6 (IQR: 3) versus 5 (IQR: 3), $p = 0.047$. When adjusted for age and ASA $p = 0.186$ FEV1 (%ppo): 72 (SD 19%) versus 71 (SD 21%), $p = 0.744$
Aguilo et al. (1997) Spain *RCT*	20 patients scheduled for elective lung resection *Sample loss*: 1 (IG) with draw from the study *Compliance*: 1 withdrawal due to nasal mask intolerance *Age (years)*: IG: 51.9 (SD 5.5) CG: 55.9 (SD 2.9) *Sex*: IG: 8 M/2 F CG: 9 M/0 F	BIPAP (nasal mask) once during 1 h in the recovery room as soon as cooperative. In- and expiratory pressure at 10 and 5 cm H_2O, respectively And standard care	*Standard care*: Standardized surgery and medication. Received 0.21 oxygen	*Time points*: 1 h after the intervention: • Atelectasis and pneumothorax • Adverse events such as: Air leaks, changed ventilatory pattern and systemic hemodynamics	*IG versus CG*: No participants showed sign of atelectasis or pneumothorax No significant differences between groups on measures of ventilatory pattern and hemodynamics
Arbane (2011) United Kingdom *RCT*	53 patients referred for lung resection (pneumectomy excluded) *Sample loss*: 2 missing (one in each group) and 1 withdrawal from IG group *Compliance*: Not described *Age (years)*: IG: 65.4 (min/max: 47–82) CG: 62.6 (min/max:32–47) *Sex*: Not reported	Twice daily mobility and strength training, from POD1 to POD5 or discharge, if earlier: Walking as able, marching on the spot, recumbent bike exercises (5–10 minutes per session), and seated leg raises with 2–4 lb ankle weights And standard care	*Standard care*: Standard anesthetic management. Additionally routine physiotherapy including: Airway clearance techniques, mobilization as able and upper limb activities at least once a day, starting from POD1	*Time points*: POD5 or at discharge, if earlier: • PPC (X-ray changes reported as pneumonia, respiratory complications requiring additional ventilatory support and/or return to high-dependency-care unit) • LOS	*IG versus CG*: PPC: 2 incidents versus 3, not statistically significant LOS: 8.9 (SD 3.3) versus 11.0 (SD 8.9), not statistically significant

(*Continued*)

Table 2. (Continued).

Author (year) Country, study design	Participants numbers, sample loss and compliance, age and sex	Intervention type and doses	Comparison Standard care, sham or no treatment	Outcomes measurements and time points	Results
Arbane et al. (2014) United Kingdom *RCT*	131 patients scheduled for lung resection *Sample loss*: Not mentioned *Compliance*: 2 reached over 5 min. cycling on POD1, increasing to a max of 30 min. on POD5. *Age (years)*: IG: 67 (SD 11) CG: 68 (SD 11) *Sex*: IG: 29 M/35 F CG: 43 M/24 F	Twice daily mobility and strength training, from POD1 to POD5 or discharge, if earlier: Bike exercise (2 minutes warm-up, increasing intensity to 13–15 RPE) for minimum of 5 minutes and aiming for 30 minutes/session. Additionally 10 repetitions of maximum load using ankle weights. And standard care	*Standard care*: Standard anesthetic management. Additionally routine physiotherapy including: Airway clearance techniques where indicated, mobilization, and upper limb activities at least once a day, starting from POD1	*Time points*: POD5 or at discharge, if earlier: • PPC (included death and transfer to critical care >72 h) • LOS	*IG versus CG*: PPC: 10 (16%) versus 16 (24%) LOS: 7.5 (P: 5–8) versus 7.1 (P: 6–8), $p > 0.05$
Barbagallo et al. (2012) Italy *RCT*	52 patients scheduled for elective lung resection *Sample loss*: 2 lost to follow-up (1 in each group) *Compliance*: 1 temporarily stopped CPAP because of claustrophobic attack *Age (years)*: IG: 69 (min/max: 24–78) CG: 65 (min/max: 37–76) *Sex*: IG: 22 M/3 F CG: 13 M/12 F	CPAP (helmet) twice during 2 h in the first 12 h postoperatively, 4 h between CPAP treatments Expiratory pressure at 8 cm H_2O And standard care (except for oxygen supply while receiving CPAP)	*Standard care*: Standardized surgery, medication and supplemental oxygen (FIO_2 0.4), rapid mobilization and chest physiotherapy once daily starting from the first postoperative day	*Time points*: Before and after each CPAP treatment, 24 h, 48 and 7 days after surgery: • Mortality • Minor PPC: Sublobar atelectasis or uncomplicated (normal gas exchange) sputum retention • Major PPC: Lobar atelectasis, complicated sputum retention, pneumonia, pulmonary embolism, ALI/ARDS • LOS • Air leaks	*IG versus CG*: LOS: 7 (min/max: 6–10) versus 8 (min/max: 7–21), $p = 0.042$ No significant difference between groups on mortality, minor/major PPC, and air leaks
Danner et al. (2012) Germany RCT	21 patients scheduled for lung resection in high risk of PPC (according to BTS guidelines) *Sample loss*: No loss to follow-up *Compliance*: Large deviation in CPAP duration and some in the CG received CPAP *Age (years)*: IG: 71.1 (SD 7.7) CG: 63.4 (SD 5.9) *Sex*: IG: 7 M/3 F CG: 9 M/2 F	CPAP (nasal or facial mask) 10 h on POD1 and POD2 + 6 h on POD3 (intermittently or continuously) Mean maximum in- and expiratory pressure of 16 mbar (≈16 cm H_2O). 4 patients received in- and expiratory pressure of 4 mbar (≈4 cm H_2O) And standard care	*Standard care*: Extended physiotherapeutic and medical optimizing program	*Time points*: Once during follow-up: • Mortality (during periprocedural stay or within 30 days) • PPC (pneumonia defined as presence of new and persisting lung infiltrate or purulent tracheal secretion with positive microbial findings;, and reintubation) • LOS	*IG versus CG*: Mortality: No incidents occurred PPC: 3 incidents versus 1, $p = 0.311$ LOS: 28.8 (SD 19.9) versus 18.9 (SD 9.0), $p = 0.306$

(*Continued*)

Table 2. (Continued).

Author (year) Country, study design	Participants numbers, sample loss and compliance, age and sex	Intervention type and doses	Comparison Standard care, sham or no treatment	Outcomes measurements and time points	Results
Frolund and Madsen (1986) Denmark *RCT*	75 patients scheduled for thoracic surgery, excluding heart and esophageal surgery *Sample loss*: 2 in the IG and 4 in the CG withdrew because of discomfort from arterial puncture *Compliance*: Median of 6–7 sessions (min/max: 3–12) a day *Age (years)*: IG: 62.1 (min/max: 19–85) CG: 63.1 (min/max: 32–88) *Sex*: IG: 35 M/20 F CG: 30 M/25 F	10 minutes sessions of PEP (facial mask) minimum once every waking hour, 72 h postoperatively (supervised by physiotherapist twice daily) Median expiratory pressure at 10 cm H_2O (R: 9–12) And standard care	*Standard care*: Rapid mobilization, including walking on POD1, coughing exercises, arm exercises (supervised by physiotherapist twice daily) *Sham treatment*: 10 minutes sessions of deep breathing in PEP-mask without expiratory resistance	*Time points*: POD1, POD4, and POD8, and whenever complication was expected: • Atelectasis Adverse events	*IG versus CG*: Atelectasis: 13 incidents versus 8, $p > 0.05$ Adverse events: The prevalence of cardiac arrhythmias, primarily arterial fibrillation, was the same in both groups, $p > 0.05$
Garutti et al. (2013) Spain *RCT*	110 patients undergoing lung resection by lateral thoracotomy *Sample loss*: 2 in the IG refused CPAP in the first half hour *Compliance*: cf. sample loss *Age (years)*: IG: 56 (min/max: 17–77) CG: 62 (min/max: 29–74) *Sex*: IG: 27 M/8 F CG: 32 M/8 F	CPAP (facial mask) once during 6 h when arriving at the recovery room Expiratory pressure at 5-7 cm H_2O. And standard care (except for oxygen supply while receiving BiPAP)	*Standard care*: Standard anesthetic management. Supplemental oxygen (FIO_2 = 0.35–0.5, allowing an SpO_2 > 90%)	*Time points*: Once during follow-up: • Mortality (>30 days) • LOS • PPC (>hospital discharge): Atelectasis, pneumonia and fibrobronchoscopy. • Air leaks (length of drainages in days)	*IG versus CG*: Mortality: 1 versus 0 deaths LOS: 8 (SD 4) versus 7.6 (SD 3) PPC: Atelectasis: 7 versus 9 incidents Pneumonia: 4 versus 4 incidents Fibrobronchoscopy: 0 versus 1 Air leaks: 5.7 (SD 6) versus 3.6 (SD 3)
Lorut et al. (2014) France *RCT*	360 COPD (moderate to severe) patients scheduled for lung resection *Sample loss*: 11 lost to follow-up *Compliance*: 83% (5 withdrew and 10 did not complete all sessions of BIPAP *Age (years)*: IG: 63.6 (SD 9.7) CG: 63.7 (SD 8.8) *Sex*: IG: 135 M/46 F CG: 141 M/38 F	BIPAP (facial or nasal mask) for 1 h, six times during the first 48 h postoperatively In- and expiratory pressure at 8 and 4 cm H_2O, respectively (adjusting inspiratory pressure to achieve RR < 25) And standard care	*Standard care*: Standard anesthetic management. Aerosolized therapy and supplemental oxygen (to achieve oxygen saturation level >92%). Early chest physiotherapy to assist bronchial drainage, and mobilization starting from POD1	*Time points*: Once – within 30 days postoperatively: • Acute respiratory events (ARE) defined by at least 2 of the following: RR>30, PaO_2/FiO_2 < 200 mmHg, $PaCO_2$ increase of >10 mmHg above baseline postop. value, or new x-ray infiltrate • Acute respiratory failure (ARF) defined by at least 2 of the following: Respiratory acidosis, SpO_2 < 90% or PaO_2 < 60 mmHg on 8L O_2 /min., RR>30 or clinical signs • Mortality • LOS • Persistent air leaks	*IG versus CG*: ARE: 57 (31.5%) versus 55 (30.7%), $p = 0.93$ ARF: 34 (18.8%) versus 44 (24.5%), $p = 0.20$ Mortality: 4 (2.2%) versus 9 (5%), $p = 0.16$ LOS: 18.6 (SD 40.7) versus 16.0 (SD 30.3), $p = 0.27$ Persistent air leaks: 17 versus 14, $p = 0.70$

(*Continued*)

Table 2. (Continued).

Author (year) Country, study design	Participants numbers, sample loss and compliance, age and sex	Intervention type and doses	Comparison Standard care, sham or no treatment	Outcomes measurements and time points	Results
Ludwig et al. (2011) Germany *Quasi-RCT*	135 patients undergoing lung resection *Sample loss*: Not described *Compliance*: Not described *Age (years)*: IG + CG: 62 (min/max: 40–90) *Sex*: IG + CG: 72 M/63 F	IPPB (mouth piece) for 10–20 minutes min 3 times daily, starting on the morning the first postoperative day and continuing until discharge Positive pressure of 15–20 mmHg (≈20–27 cm H_2O) And standard care	*Standard care*: Standardized surgery and physiotherapeutic rehabilitation. Rehabilitation starting the first day postoperatively, including: Pressure expiration, diaphragmatic breathing, postural correction, stretching, and shoulder girdle motion. Early mobilization was favored whenever possible at the bedside	*Time points*: Once postoperatively – within discharge: • PPC (secretion retention, pneumonia, air leaks (>7 days), pleural infection, and chest tube drainage) • LOS 7 days after surgery: • FEV^1 (% of predicted) • Change in FEV1	*IG versus CG*: PPC: 15 versus 15 LOS: 11 (min/max: 6–37) versus 11 (min/max: 5–41) FEV1: 52% (R:39–106) versus 45% (R:24–79) Change in FEV^1: −27% (min/max: −68–5) versus −23% (min/max: −61–49)
Nery et al. (2012) Brazil *Quasi-RCT*	30 patients undergoing elective lung resection *Sample loss*: Not described *Compliance*: All patients tolerated CPAP application well *Age (years)*: IG: 55 (SD 12.3) CG: 56.8 (SD 10.2) *Sex*: IG: 11 M/4 F CG: 10 M/5 F	CPAP (facial mask) for 30 minutes twice daily starting on the first postoperative day until the 7th postoperative day Expiratory pressure at 10 cm H_2O And standard care	*Standard care*: Twice a day of breathing exercises (10 ventilatory cycles, with a 15–30 second interval between cycles)	*Time points*: Daily: • Pneumonia • Atelectasis • Pneumothorax 7 days after surgery: • Lung function (Peak expiratory flow, maximal inspiratory and expiratory pressure, FVC, FEV1)	*IG versus CG*: No participants showed sign of pneumonia, atelectasis, or pneumothorax FVC (L): 2.28 (SD 0.80) versus 1.81 (SD 058), $p = 0.09$ FEV1 (L): 1.59 (SD 0.55) versus 1.42 (SD 0.43), $p = 0.23$
Reeve et al. (2010) New Zealand	76 patients undergoing elective lung resection via open thoracotomy *Sample loss*: No loss to follow-up *Compliance*: Intervention were provided as scheduled on 81% of occasions *Age (years)*: IG: 63.1 (SD 12.5) CG: 65.1 (SD 11.0) *Sex*: IG: 26 M/16 F CG: 21 M/13 F	Targeted respiratory physiotherapy twice daily until discharge: • Deep breathing • Coughing exercises • Assistance with ambulation • A progressive shoulder and thoracic cage mobility program And standard care	*Standard care*: Standardized clinical pathway including usual medical and nursing care, early and frequent position changes in bed and early ambulation. Receiving an exercise booklet preoperatively providing nonspecific advice regarding postoperative exercises	*Time points*: Once during follow-up: • PPC (≥4 of: Atelectasis, elevated white blood cell count or use of respiratory antibiotics, temperature >38 C, sign of infection on sputum microbiology, oxygen saturation <90% on room air, purulent sputum production, diagnosis of pneumonia, readmission to ICU due to respiratory problems) • Mortality • LOS	*IG versus CG*: PPC: 2 (4.8%) incidents versus 1 (2.9%), $p = 1.00$ Mortality: 1 (2.4%) versus 0 (0%) LOS: 6.0 (IQR: 4.0) versus 6.0 (IQR: 1.0), $p = 0.87$ No adverse events were reported

(*Continued*)

Table 2. (Continued).

Author (year) Country, study design	Participants numbers, sample loss and compliance, age and sex	Intervention type and doses	Comparison Standard care, sham or no treatment	Outcomes measurements and time points	Results
Roceto (2014) Brazil	40 patients scheduled for lung resection with posterolateral thoracotomy due to lung cancer *Sample loss*: No loss to follow-up *Compliance*: 1 showed intolerance to CPAP *Age (years)*: IG: 60.4 (SD 8.9) CG: 56.1 (SD 10.7) *Sex*: IG: 13 M/7 F CG: 10 M/10 F	CPAP (nasal mask) for 2 h. Once on the day of surgery and twice daily on the 1st and 2nd postoperative day Pressure starting between 7–8.5 cm H_2O (adjusting pressure to achieve RR<30) And standard care	*Standard care*: Standardized surgical and anesthetic management and chest physiotherapy including: Bronchial hygiene techniques and deep diaphragmatic breathing exercises. Supplemental oxygen to maintain SpO_2 > 90%	*Time points*: Once during follow-up: • LOS Once on DoS, POD1, POD2, and POD5 or day of discharge: • Air leaks	*IG versus CG*: (Only *p*-values were reported) Air leaks: Significantly more air leaks in the IG on DoS and POD1, $p = 0.001$ and $p = 0.028$ respectively, but not significantly on the days hereafter Lung function was not reported post intervention.

ALI = Acute lung injury
ARDS = Acute respiratory distress syndrome
ASA = American society for anesthesiologists score
BIPAP = Bilevel positive airway pressure
CG = Control group
CPAP = Continuous positive airway pressure
DoS = Day of surgery
F = female
FEV^1 = Forced expiratory volume in the first second
FIO_2/PaO_2 = ratio between inspired oxygen and the partial pressure of arterial oxygen
h = hour
ICU = intensive care unit
IG = Intervention group
IPPB = Intermittent positive pressure breathing
IQR = Interquartile range
IS = Incentive spirometry kPa = kilo Pascal
lb = pounds
LOS = length of hospital stay (days)
M = male
Min/max = minimum and maximum values
mmHg = millimeter mercury
SD = standard deviation
P = 25th and 75th percentiles
p = *p*-value (presented if reported in the study)
POD = postoperative day
PPC = postoperative pulmonary complications
SaO_2 = peripheral capillary oxygen saturation (invasive measure)
SpO_2 = peripheral pulse oximetry (non-invasive measure)
REP = maximum amount of weight one can lift in 10 repetitions
RR = respiratory rate (breath per minute)

Table 3. Overview of excluded studies [ordered by author].

Study ID	Reason for exclusion
Brocki et al. (2016)	Intervention started preoperatively (the day before surgery) and continued two weeks postoperatively (proceeding beyond hospital discharge).
Chang et al. (2014)	Study design was not a randomized controlled trial. Intervention was a 12-week rehabilitation program (proceeding beyond hospital discharge) consisting of aerobic and strength exercises
Chatham (1993)	Study design was not a randomized controlled trial.
Cho et al. (2014)	Intervention was comparison of two methods of breathing exercises/devices. The study did not include any control group receiving no treatment, sham treatment or standard care.
Gosselink et al. (2000)	Study population included patients undergoing lung and esophageal resection (results for patients undergoing lung resection were not presented separately).
Granger et al. (2013)	Intervention was a twice daily exercise until discharge and twice weekly as outpatient for 8 weeks (proceeding beyond hospital discharge. No measuring of outcomes at hospital discharge).
Ingwersen et al. (1993)	Intervention was comparison of three face mask systems (PCAP, PEP, and IR-PEP) used in addition to respiratory physiotherapy. The study did not include any control group receiving no treatment, sham treatment or standard care.
Jan et al. (1976)	Study design was not a randomized controlled trial. Study population included children as young as 7 years of age.
Park et al. (2012)	Intervention was comparison of two methods of vibration (one mechanical and one manual). The study did not include any control group receiving no treatment, sham treatment or standard care.
Vilaplana et al. (1990)	The study population included patients undergoing lung and esophageal resection (results for patients undergoing lung resection were not presented separately).

Gosselink et al., 2000; Granger et al., 2013; Ingwersen et al., 1993; Jan, Lien, and Hsieh, 1976; Park et al., 2012; Vilaplana et al., 1990) are presented in Table 3.

Risk of bias of the included studies

Five studies had low risk of bias (Arbane et al., 2014; Arbane, Tropman, Jackson, and Garrod, 2011; Garutti et al., 2014; Lorut et al., 2014; Reeve et al., 2010); three studies had unclear risk of bias (Agostini et al., 2013; Aguiló et al., 1997; Barbagallo et al., 2012); and five studies had high risk of bias (Danner et al., 2012; Frolund and Madsen, 1986; Ludwig et al., 2011; Nery et al., 2012; Roceto, Galhardo, Saad, and Toro, 2014) (Figure 2).

The evaluation of risk of bias of the included studies is clarified in the following section according to the domains of the Cochrane risk of bias tool. Randomization and allocation biases were found in two trials (Ludwig et al., 2011; Nery et al., 2012). These trials were considered quasi-randomized due to the used randomization methods in form of date of birth and sequentially allocation one by one, which made it impossible to conceal group allocation. Six studies did not describe the randomization and/or allocation methods and were rated as unclear risk of bias (Agostini et al., 2013; Aguiló et al., 1997; Barbagallo et al., 2012; Danner et al., 2012; Frolund and Madsen, 1986; Roceto, Galhardo, Saad, and Toro, 2014).

Blinding of patients and personnel were the source of high risk of bias in all studies, because the patients and often the personnel were an active part of the intervention. Frolund and Madsen (1986) used a sham treatment in form of a PEP-mask without an expiratory resistance. Nevertheless, the study was classified as high risk of bias because group allocation was assessed by the review authors as being easily detectable by both patients and personnel. One study did not attempt blinding of the outcome assessors and was rated as high risk of bias (Roceto, Galhardo, Saad, and Toro, 2014). Four other studies did not describe whether the assessors of outcomes were blinded and were consequently rated as unclear risk of bias (Aguiló et al., 1997; Barbagallo et al., 2012; Danner et al., 2012; Ludwig et al., 2011).

Incomplete outcome data was rated as unclear risk of bias in one study due to lacking information on missing data, patient exclusions, and withdrawals from the study (Ludwig et al., 2011). The remaining studies had very few withdrawals or missing data and the risk of bias was rated as low.

Selective reporting was evaluated as low in three studies, which were registered in the ISRCTN registry (Arbane et al., 2014; Lorut et al., 2014; Reeve et al., 2010). All three studies reported the pre-specified outcome measures. Concerning the remaining 10 studies, 1 study was rated as having high risk of bias for selective reporting: Ludwig et al. (2012) included an investigation of whether intermittent positive pressure breathing (IPPB) could prevent atelectasis of the operated lung; however, this outcome was not reported.

Other potential sources of bias were found in relation to compliance of allocated intervention; baseline imbalances; exclusion of outcome events; and obscure methodology was assessed as potential biases.

Compliance of intervention was found in Danner et al. (2012), who investigated the intervention of CPAP compared to a control group receiving standard treatment. However, the control group received 0.6 (SD 1.4) hours of CPAP on the day of operation, 0.4 (SD 0.9) hours on the first postoperative day, and 0.4 (SD 1.0) hours on

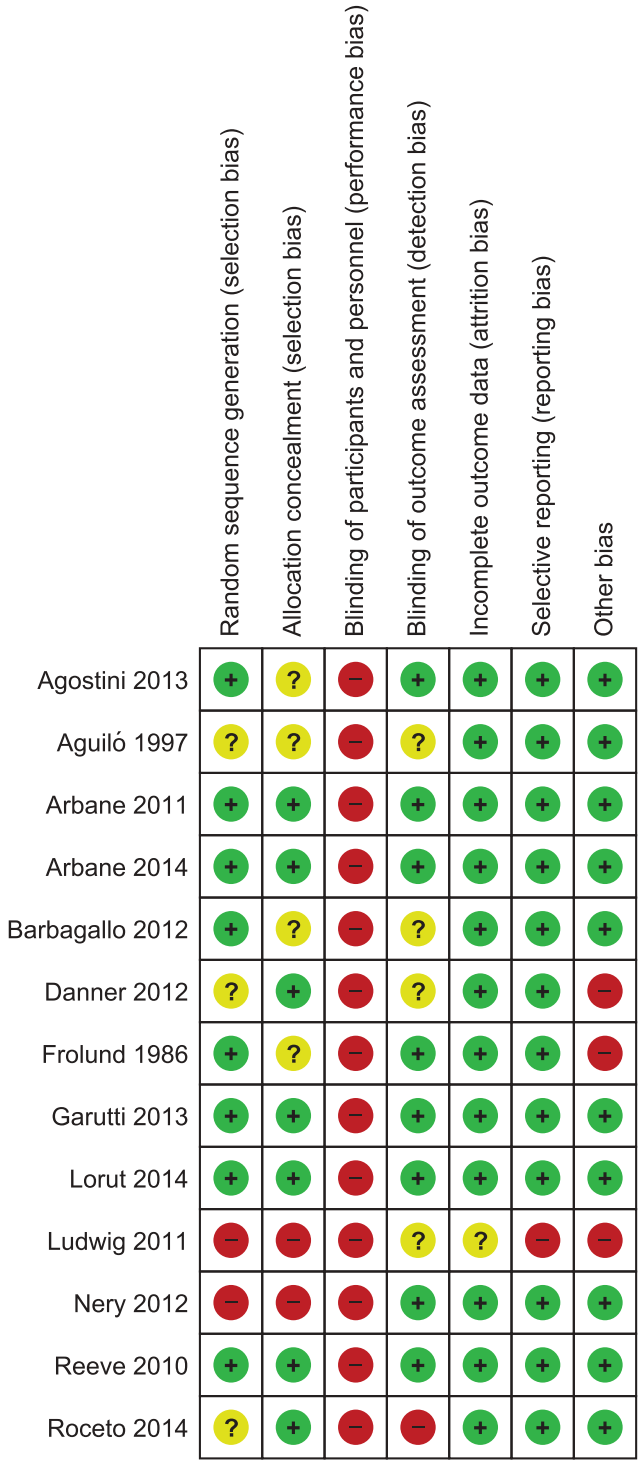

Figure 2. Summary of risk of bias assessment of the included studies.

the second postoperative day. This suggests contamination of the standard treatment, and therefore the risk of bias was rated as high.

Baseline imbalances were a potential risk of bias in two studies (Danner et al., 2012; Frolund and Madsen, 1986). In the study by Danner et al. (2012), the control group was generally younger and their predicted postoperative lung function was lower than in the intervention group. Since patients with a high preoperative lung function do not achieve as high relative improvements after surgery compared to patients with a low preoperative lung function, this imbalance may have biased the effect of CPAP. Accordingly, the study was rated as high risk of bias. In the study by Frolund and Madsen (1986), more pneumectomies were performed in the control group than the intervention group. The probability of having atelectasis after a pneumectomy is lower than after a segment resection or explorative thoracotomy, and may have affected the rate of atelectasis, for which reason the study was rated as high risk.

Exclusion of outcome events were done in the study by Frolund and Madsen (1986), who investigated the effect of PEP on the outcomes hypoxemia and atelectasis. They did, however, exclude patients who received oxygen because of a PaO_2 less than 5 kPa despite the fact that low oxygenation can be caused by atelectasis. In the control group, six patients were offered oxygen and four of these showed signs of atelectasis, while four patients in the intervention group were offered oxygen and one of them showed signs of atelectasis. The difference in rate of atelectasis between the groups would have been less if they had not excluded these patients and therefore the study was rated as high risk of bias.

Obscure methodology was a problem in the study by Ludwig et al. (2011), which generally was difficult to assess in aspects of risk of bias because the method section was sparse. Therefore, the review authors rated the risk of bias as high.

Outcomes

Mortality

Seven studies reported mortality rates (Agostini et al., 2013; Barbagallo et al., 2012; Danner et al., 2012; Garutti et al., 2014; Lorut et al., 2014; Ludwig et al., 2011; Reeve et al., 2010). Five studies reported in-hospital mortality, and only two measured death within 30 days (Lorut et al., 2014; Reeve et al., 2010). In general, the mortality rate was very low, and two studies had no incidents of death (Danner et al., 2012; Ludwig et al., 2011). The meta-analysis showed no difference in mortality when given CPAP (RR 0.77; 95%CI 0.22–2.67) (Figure 3). Using the GRADE criteria, the level of evidence was downgraded two levels due to very serious imprecision based on the very small number of events and the large CI of the estimate. Additionally, there was no difference in rate of mortality when given incentive spirometry (RR 0.32; 95%CI 0.01–7.73) or targeted respiratory physiotherapy (RR 2.44; 95%CI 0.10–58.10) when compared with standard care.

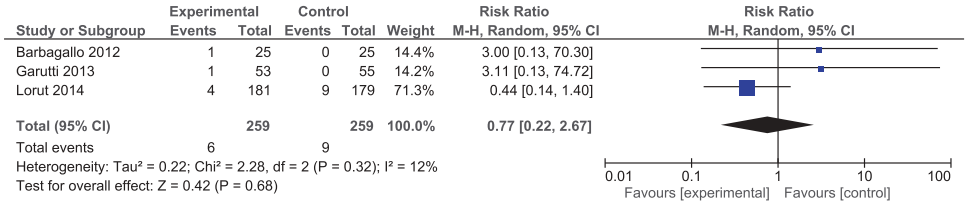

Figure 3. Forest plot of respiratory physiotherapy in addition to standard treatment vs. standard treatment alone on the outcome mortality.

Lorut 2014: Measured mortality within 30 days. The other studies reported in-hospital mortality.

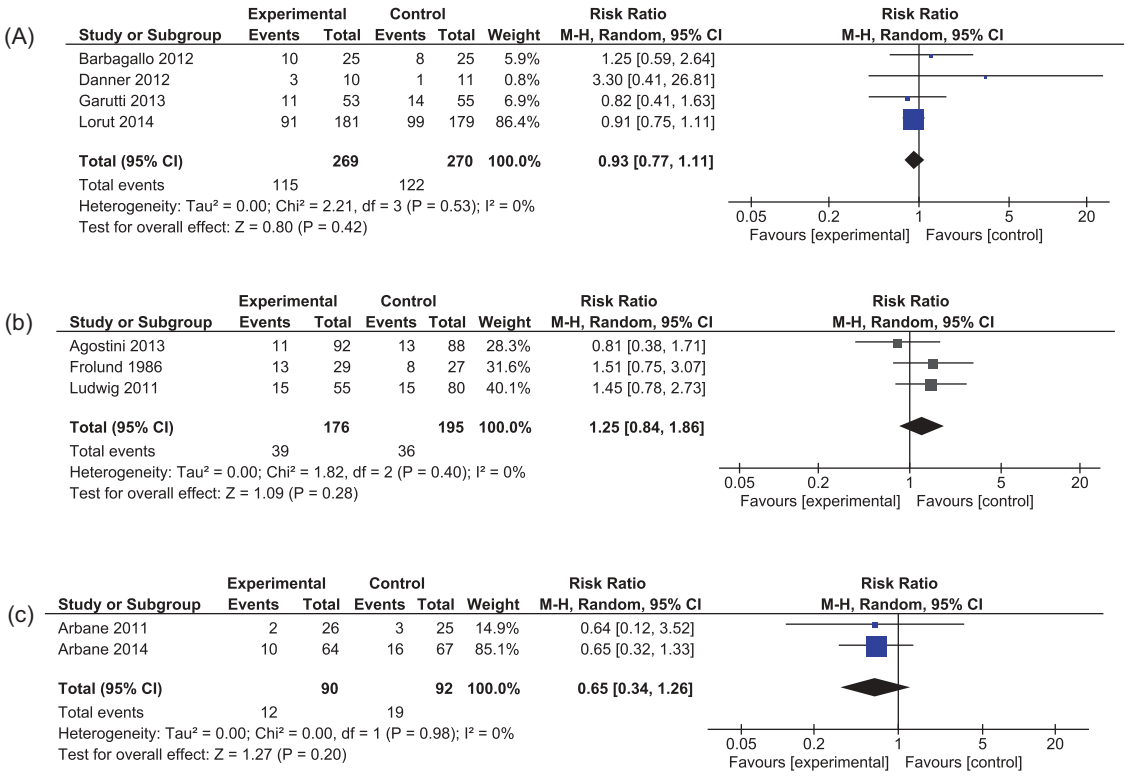

Figure 4. Forest plot of respiratory physiotherapy in addition to standard treatment vs. standard treatment alone on the outcome postoperative pulmonary complications (PPC).

Garutti 2013: Atelectasis, pneumonia and fibrobronchoscopy are combined as PPC in this analysis.

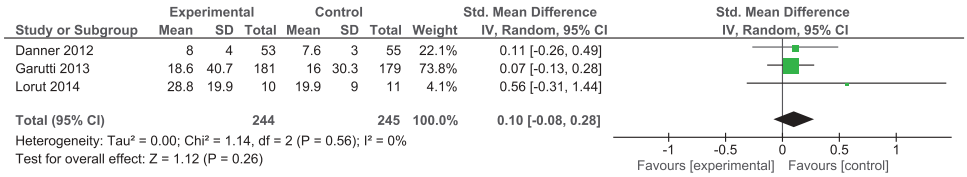

Figure 5. Forest plot of CPAP in addition to standard treatment vs. standard treatment alone on the outcome length of hospital stay (LOS).

Postoperative pulmonary complications (PPC)

Twelve studies evaluated PPC or constituent elements of PPC (Agostini et al., 2013; Aguiló et al., 1997; Arbane et al., 2014; Arbane, Tropman, Jackson, and Garrod, 2011; Barbagallo et al., 2012; Danner et al., 2012; Frolund and Madsen, 1986; Garutti et al., 2014; Lorut et al., 2014; Ludwig et al., 2011; Nery et al., 2012; Reeve et al., 2010). As seen in Table 2, the definition of PPC varied among the studies, and three trials solely observed constituent elements, such as atelectasis or pneumonia based on X-ray examinations (Aguiló et al., 1997; Frolund and Madsen, 1986; Nery et al., 2012). Two studies did not detect any incidents of

Table 4. Narrative synthesis of respiratory physiotherapy in addition to standard treatment vs. standard treatment alone on the outcome length of hospital stay (LOS).

Study	Intervention	Control	*P*-value
CPAP			
Barbagallo et al. (2012)	7 (Min/max: 6–10)	8 (Min/max: 7–12)	$P < 0.05$
Breathing exercises			
Ludwig et al. (2011)	11 (Min/max: 6–37)	11 (Min/max: 5–41)	NS
Agostini et al. (2013)	6 days (IQR: 3)	5 days (IQR: 3)	NS when adjusted for baseline imbalances (age and ASA-score > 3)
Exercise			
Arbane et al. (2014)	7.5 days (P25-P75: 5–8)	7.1 days (P25-P75: 6–8)	NS
Arbane (2011)	8.9 days (SD 3.3)	11 days (SD 8.9)	NS
Targeted respiratory Physiotherapy			
Reeve et al. (2010)	6.0 (IQR: 4.0)	6.0 (IQR: 1.0)	NS

IQR = interquartile range, min/max = minimum and maximum values, P25-P75 = 25th and 75th percentiles, SD = standard deviation, NS = not significant.

PPC (Aguiló et al., 1997; Nery et al., 2012). In the study by Reeve et al. (2010), targeted respiratory physiotherapy did not show a difference in the rate of PPC (RR 1.62; 95%CI 0.15–17.10). The remaining nine studies were combined in a meta-analysis by type of respiratory physiotherapy (Figure 4a–c). Two studies investigating the effect of CPAP divided PPC into minor and major complications (Barbagallo et al., 2012; Lorut et al., 2014), and both of these were combined in the analysis. The meta-analysis did not show a significant effect on preventing events of PPC when given CPAP (RR 0.93; 95%CI 0.77–1.11), breathing exercises (RR 1.25; 95%CI 0.84–1.86), or exercise (RR 0.65; 95% CI 0.34–1.26). Sensitivity analyses including only minor or major events of PPC did not change the results. Sensitivity analyses on studies investigating CPAP showed a non-significant result of high risk studies favoring the control group (RR 3.30; 95%CI 0.41–26.81) and low risk studies favoring the experimental group (RR 0.65; 95%CI 0.14–19.01). Using the GRADE criteria, the level of evidence was downgraded one level for the subgroup 'CPAP'. The downgrading was due to high risk of bias in two of the smaller studies – the same studies that also lacked a clear definition of PPC. The subgroup 'Breathing exercises' was downgraded two levels due to high risk of bias (the studies contributing to nearly 50% of the population had high risk of bias). The subgroup 'Exercise' was downgraded one level due to serious imprecision based on the large CI of the estimate).

There was no difference in effect of CPAP when looking at high risk patients alone (RR 1.12; CI95% 0.44–2.88) (Danner et al., 2012; Lorut et al., 2014). Additionally, two studies reported stratified analyses of the effect on different risk of PPC. The study by Agostini et al. (2013) showed no difference in the effect of IS on PPC when stratified in high and low-risk groups. Garutti et al. (2014) investigated the effect of CPAP when stratified in five groups with different risk of developing postoperative pneumonia but found no difference on incidences of pneumonia or atelectasis.

Length of stay (LOS)

Nine studies evaluated LOS (Agostini et al., 2013; Arbane et al., 2014; Arbane, Tropman, Jackson, and Garrod, 2011; Barbagallo et al., 2012; Danner et al., 2012; Garutti et al., 2014; Lorut et al., 2014; Ludwig et al., 2011; Reeve et al., 2010). Three studies, investigating CPAP, reported LOS using means and SDs, and these results were combined in a meta-analysis (Figure 5). The results showed no difference in LOS when given CPAP (MD 0.88; 95%CI −1.45 to 3.22).

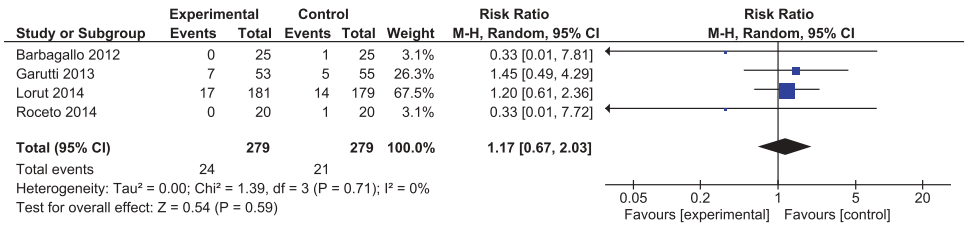

Figure 6. Forest plot of CPAP in addition to standard treatment vs. standard treatment alone on the outcome air leak (adverse events).

Barbagallo 2012: Air leak was measured as number of patients having air leaks on the 7th postoperative day.

Garutti: 2013 Air leak was measured as number of patients having air leaks on the 7th postoperative day. Data was obtained from author correspondence.

Lorut 2014: Air leak was measured as number of patients with air leaks >4 days, and/or air leaks interfering with the ability to ventilate correctly.

Using the GRADE criteria, the level of evidence on CPAP was downgraded one level due to serious imprecision based on the large CI of the estimate.

The remaining six studies were summarized in a narrative synthesis (Table 4). Barbagallo et al. (2012) was the only study reporting a statistically significant difference in LOS between the groups (p = 0.042). When looking at studies of high risk patients, prophylactic CPAP did not significantly shorten LOS (MD 4.30; 95%CI −2.18 to 10.79) (Danner et al., 2012; Lorut et al., 2014).

Lung volume and function

Three studies evaluated the effect on lung volume and function on the fourth to the seventh postoperative day (Agostini et al., 2013; Ludwig et al., 2011; Nery et al., 2012). The study of Ludwig et al. (2011), investigating the effect of CPAP, reported a forced expiration volume in the first second (FEV1) of 45% (range 24–79) in the intervention group versus 52% (range 27–77) in the control group on the seventh postoperative day. Nery (2012), also investigating CPAP, found no difference in FEV1 (MD 0.34; 95%CI −0.39 to 1.06). Additional measurements such as forced vital capacity, peak flow, and maximal in- and expiratory flow did not show any difference in lung volume and function either, however, the sample size was small. Nor did the study by Agostini et al. (2013), investigating incentive spirometry, show a difference in FEV1 (0.05; 95%CI −0.24 to 0.36).

Adverse events

Six studies (Agostini et al., 2013; Barbagallo et al., 2012; Garutti et al., 2014; Lorut et al., 2014; Nery et al., 2012; Roceto, Galhardo, Saad, and Toro, 2014), which investigated different types of positive pressure breathing, evaluated whether the intervention prolonged the presence of air leaks. Nery et al. (2012) measured air leaks on the seventh postoperative day, and found no incidents of prolonged air leaks. Ludwig et al. (2011) found no significant difference in air leaks after the seventh postoperative day when given intermittent positive pressure breathing (RR 1.16; 95%CI 0.33–4.14). The results from the remaining four studies were combined in a meta-analysis (Figure 6), which showed no difference in air leaks between the fifth and the seventh day when given CPAP (RR 1.17; 95%CI 0.67–2.03). Using the GRADE criteria, the level of evidence was downgraded two levels: one level due to high risk of bias in two smaller studies; and one level due to serious imprecision based on the large CI of the estimate.

According to time of measurement, Roceto, Galhardo, Saad, and Toro (2014) found a significantly higher rate of air leaks in the CPAP group than in the control group on the day of surgery (RD 60; 95%CI 35.4–84.0) and the first postoperative day (RD 35; 95%CI 7.0–63.0), but no difference on the fifth postoperative day (based on author information). Also, Barbagallo et al. (2012) stated that most air leaks spontaneously disappeared on the fifth postoperative day.

In respect to other adverse events, incidents such as skin damage (Lorut et al., 2014); ventilatory pattern (Aguiló et al., 1997); hemodynamics (Aguiló et al., 1997; Frolund and Madsen, 1986; Nery et al., 2012); and gastric distension (Lorut et al., 2014) were measured, but none of these adverse events were observed. Garutti et al. (2014) reported that one patient experienced the pressure of the CPAP-mask as painful, but the symptom stopped immediately after termination of treatment. Three other studies reported single events of intolerance with CPAP treatment because of claustrophobic attack (Aguiló et al., 1997; Barbagallo et al., 2012; Roceto, Galhardo, Saad, and Toro, 2014).

Assessment of publication bias

There was a tendency towards smaller studies showing a negative effect rather than a positive effect which is why the authors did not suspect publication bias.

Discussion

Summary of main results

Various types of respiratory physiotherapy, such as positive pressure breathing, deep breathing exercises, and strength and aerobic exercises as a supplement to standard care show no significant effect over standard care alone in preventing mortality or PPC, reducing LOS, or improving lung volume and function. Neither did analyses on high risk groups alone show an effect of CPAP on preventing PPC. The mortality rate was low, and the majority of deaths occurred in a larger multicenter study including only patients at high risk of PPC (Lorut, 2014).

The studies investigating CPAP, BIPAP, or IPPB showed no difference in prolonged air leaks on the fifth to seventh postoperative day. However, studies were probably too small to detect serious adverse events. Furthermore, it is still unknown if these interventions may increase the incidents of air leaks earlier on.

Overall completeness and applicability of evidence

The results were presented for subgroups of intervention, because the included studies investigated different types of respiratory physiotherapy. Still, the timing and duration of the intervention varied within the subgroups. Overall, standard care seemed adequate compared to the experimental intervention. The studies investigating CPAP did not describe which respiratory physiotherapy modalities were used as standard care and the dose of treatment. Thus, it is difficult to evaluate standard care as a frame of reference. However, in the majority of the studies standard care entailed early mobilization, breathing exercises and airway clearance techniques (not specified). Perhaps standard care is even to excessive in the pursuit of preventing PPC among patients undergoing lung resection, or maybe standard care is simply effective in preventing PPC. Only one study by Reeve et al. (2010) investigated respiratory physiotherapy as a package compared to standard care without any physiotherapy. This study did not show a larger effect of respiratory physiotherapy than studies investigating constituent elements of respiratory physiotherapy. However, the study population was small, and further trials of similar design are needed to make any final conclusions. Regardless, the outcome PPC is difficult to measure and one of the challenges of assessing the effect of respiratory physiotherapy is the variance of and lack of consensus on the definition of PPC. In all probability, a randomized trial will additionally be challenged by ethical considerations and a low participation rate because the patients risked being allocated to a control group given less treatment.

In general, the transferability of the results of our review appears satisfactory due to the fact that all studies included patients undergoing lung resection. However, since half of the included studies did not describe how many patients were assessed for eligibility, the assessment of representability of the study populations was challenged. The comparison between populations of high and low risk of PPC was not possible in this review. Two studies investigating CPAP included high risk populations but none of the other studies investigating CPAP were considered strictly low risk populations.

Quality of the evidence

The quality of evidence based on the GRADE approach was generally evaluated to be moderate to low. The level of evidence on the outcome mortality and adverse events measured as air leaks was rated as low. The level of evidence on the outcome LOS and PPC was rated as moderate, with the exception of the subgroup 'Breathing exercises' for PPC, which was rated as low. None of the studies were able to blind participants and personnel due to the nature of the intervention. Additionally, downgrading of the level of evidence was due poor study methodology and imprecision.

Potential biases in the review process

Two studies including a mixed population of esophageal and lung resections were excluded, because the results were not presented separately for patients undergoing lung resection (Gosselink et al., 2000; Vilaplana et al., 1990).

Several authors did not respond to our request for further information required for bias assessment or e.g. means and SDs on LOS, which implied that these studies could not be included in the meta-analysis (Agostini et al., 2013; Arbane et al., 2014; Barbagallo et al., 2012; Ludwig et al., 2011; Reeve et al., 2010). Overall, the results of these studies did not differ considerably from the studies included in the meta-analysis on LOS. One study identified in the ISRCTN registry had not been published before the completion of this review, but should be included in a future update concerning this topic.

The definition of PPC differed among the included studies, and several studies did not have PPC as a primary outcome (Aguiló et al., 1997; Arbane et al., 2014; Arbane, Tropman, Jackson, and Garrod, 2011; Frolund and Madsen, 1986; Nery et al., 2012). Three studies solely observed atelectasis, pneumothorax, or pneumonia based on X-ray examinations, and one study did not specify the definition of PPC. This could induce a risk overlooking events of PPC and thereby underestimate the effect of respiratory physiotherapy. Sensitivity analyses, however, did not show any difference in effect when comparing high and low risk of bias studies. This is in accordance with studies having a clear and well-defined clarification of PPC compared with studies only measuring elements of PPC. Furthermore, sensitivity analyses showed no difference when PPC was measured as major or minor PPC. The risk of bias concerning the definition and measurements of PPC was taken into account when grading the quality of evidence in the GRADE analysis.

Agreements and disagreements with other studies or reviews

Other reviews related to respiratory physiotherapy after lung resection reported similar results as the current review. Rodriguez-Larrad, Lascurain-

Aguirrebena, Abecia-Inchaurregui, and Seco (2014) concluded that in general interventions performed only during the postoperative period did not seem to reduce PPC or LOS. Furthermore, a Cochrane review by Torres, Porfirio, Carvalho, and Riera (2015) investigating the effect of CPAP showed that CPAP was safe but had no effect on reducing the rate of mortality, PPC, or LOS. The authors did however query the results considering the low quality of evidence and small sample sizes with few events. In a literature review of 2017, the authors likewise concluded that the effect of breathing exercises involving external devices, such as IS and PEP was questionable (Kendall et al., 2017). The authors questioned the quality of evidence from the study of Reeve et al. (2010) (included in the current review), given that all study participants had good lung function and the presence of baseline imbalances (i.e. the experimental group being more overweight) could induce an underestimation of the effect of respiratory physiotherapy. Kendall et al. (2017) cautioned against concluding that respiratory physiotherapy had no effect altogether. Instead they highlighted the importance of routine interventions during the postoperative period, including maximal inspiratory exercises, coughing, and mobilization exercises of the upper and lower limps under supervision. This recommendation was based on two observational studies, performed on the same cohort of patients, conducted by Varela et al. (2006) and Novoa et al. (2011).

Conclusions

Implications for practice

Prophylactic treatments consisting of large doses of CPAP does not seem to affect the rate of mortality and PPC, when compared with standard care. This review indicates that it may not be relevant to offer CPAP to patients undergoing lung resection surgery if they receive standard care embodying respiratory physiotherapy modalities, such as airway clearance techniques and assistance with early ambulation. However, further research is still needed to make a final conclusion. The effect of standard respiratory physiotherapy as a package is still unknown, and may or may not be effective in preventing PPC among patients undergoing lung resection.

Implications for research

This systematic review visualizes the need for larger trials of better methodological quality (e.g. blinding of outcome assessment, detailed description of standard care, clear definition of PPC and relevant time point measurements). To a greater extent, there is a need for trials including a control group receiving standard care without any respiratory physiotherapy modalities.

Differences between protocol and review

Two authors, and not three as described in the protocol, performed the study selection and data extraction due to limited time resources. A third author was involved if necessary. Additionally, the search terms 'thoracotomy' and 'inspiratory muscle training' were added to the search strategy presented in the review protocol.

Disclosure Statement

The authors report no conflict of interest.

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